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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,689	WILLIAMS, JOHN G.K.	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *4-17,20,21,24,25 and 27-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,18,19,22,23 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 7, 2008 has been entered.

2. Claims 1-46 were previously pending, with claims 4-17, 20, 21, 24, 25 and 27-46 withdrawn from consideration.

3. Applicant amended claims 1 and 29. Claims 1-3, 18, 19, 22, 23 and 26 will be examined.

4. Applicant's amendments overcame the rejection of claims 1-3, 18, 19 and 26 under 35 U.S.C. 102(b) as anticipated by Yao et al. All other previously presented rejections are maintained for reasons given in the "Response to Arguments" section below.

5. This office action contains new grounds for rejection.

Response to Arguments

6. Applicant's arguments filed November 17, 2008 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1-3, 18 and 26 under 35 U.S.C. 102(a) as anticipated by Motz et al., Applicants argue that Motz et al. do not teach covalent attachment of an anchor to the polymerase, that the PCNA molecule of Motz et al. has the same properties as other PCNA molecules, and therefore recycling of PCNA is not an irreversible association as claimed.

With regard to the covalent attachment of an anchor, Motz et al. specifically teach a Taq DNA polymerase covalently modified with an anchor molecule containing a PCNA-binding motif, which

leads to the formation of an attachment complex comprising the modified polymerase and PCNA, and results in an increased processivity of the Taq polymerase (Fig. 4; page 16181, last paragraph; page 18182, first and second paragraphs). Further, there is no requirement in the claims that the attachment complex be covalently bound to the polymerase. Finally, there no structural requirements in the claims as to the nature of the "anchor" or the "attachment complex", they are claimed in terms of their function only. Motz et al. teach using a modified Taq DNA polymerase which incorporates a binding site for the PCNA protein. Therefore, after addition of PCNA, which then binds to the Taq polymerase and stays bound during the replication process, the processivity of the polymerase is increased as a result, since the presence of PCNA prevents the target nucleic acid from diffusing away from the polymerase during replication, therefore irreversibly associating the polymerase with the target nucleic acid during the replication process, as required by the claims. The fact that PCNA is recycled outside of the replication process is irrelevant to the claimed subject matter.

The rejection is maintained.

B) Regarding the rejection of claims 19 and 22 over Motz et al. and Blanco et al., Applicants argue that Motz et al. does not suggest claim 1, therefore the rejection is improper. This argument was addressed above.

The rejection is maintained.

C) Regarding the rejection of claim 23 under 35 U.S.C. 103(a) over Williams and Motz et al. Applicants argue that since claim 1 is patentable, it cannot be obvious.

The patentability (or lack thereof) of claim 1 was addressed above.

The rejection is maintained.

Claim Interpretation

7. The term "attachment complex" has not been defined by Applicant, therefore it is considered as any molecule. Further, the term "polymerase has an attachment complex" is interpreted as "polymerase comprises an attachment complex" and the attachment complex may be covalently or non-covalently linked to the polymerase. Further, according to claim language, the anchor may be considered as the attachment complex.

8. In view of Applicant's amendment reciting "an attachment complex comprising at least one anchor covalently attached thereto" and indefiniteness of this limitation (because it is not clear whether the anchor is covalently attached to the polymerase or to other parts of an attachment complex, see below), the limitation is interpreted as an anchor attached to the polymerase.

9. Applicant did not define the term "anchor", therefore it is considered as any molecule or a part of molecule.

10. Applicant did not define the term "modified amino acid", therefore any modification, i.e., labeling, attachment of other amino acids, etc. is considered to anticipate this term.

11. Applicant did not define the term "irreversible association", therefore, any association is considered as irreversible, provided the time scale or topological constraints.

12. Applicant defined the term "processivity index" on page 7, [0038], as the number of nucleotides sequenced divided by the number of nucleotides in the template.

Claim Rejections - 35 USC § 112, written description

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-3, 18, 19, 22, 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of polymerases none of which are disclosed in the specification in terms of their structures, i.e., their amino acid sequences. The claimed genus encompasses all possible polymerases, i.e., DNA and RNA polymerases, with the only functional limitation that the polymerase has to have an "anchor", the structure of which is not defined, covalently attached. These claims further encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations as well as proteins altered in their domain structure, and no specific amino acid sequences have been provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might

> achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the polymerase having an attachment complex comprising an anchor lack any specific structure, and is precisely the situation of naming a type of material which is generally known to likely exist, but is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "a polymerase-nucleic acid complex comprising a polymerase having an attachment complex comprising an anchor", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a polymerase comprising an attachment complex, without any definition of the particular polymerase claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any polymerases as claimed. Therefore, the claims fail to meet the written description requirement by encompassing polymerases which are not described in the specification.

Claim Rejections - 35 USC § 112, enablement

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-3, 18, 19, 22, 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 1-3, 18, 19, 22, 23 and 26 are broadly drawn to a polymerase-nucleic acid complex, in which the polymerase comprises an attachment complex which comprises at least one anchor covalently attached to the polymerase. However, as will be further discussed, there is no support in the specification and prior art for the structure as claimed. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Working Examples

The specification has no working examples of any polymerases comprising an attachment complex which irreversibly associates the polymerase with a target nucleic acid.

Guidance in the Specification.

The specification provides no evidence that the claimed polymerase can be produced as claimed. The only mention of any specific polymerase is in paragraph [0050] and [0051] on pages 11 and 12, where it mentions a Therminator polymerase (no specific amino acid sequence provided) which has two peptides attached to amino acid positions K53 and K229. No such polymerase was produced by Applicant and there is no evidence that it would function as claimed. Considering the large number of polymerases with differing structures and function, i.e., DNA- and RNA-dependent DNA polymerases and RNA- and DNA-dependent RNA polymerases, for example, the guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

The unpredictability of the art and the state of the prior art

There is a great deal of unpredictability in the modification of structural properties of polymerases, due to the diversity of their amino acid sequences and corresponding three-dimensional structures. As evidenced by Braithwaite et al. (Nucl. Acids Res., vol. 21, pp. 787-802, 1993), in 1993 there were three families of DNA polymerases (A, B and C) and about 56 known amino acid sequences (page 787, Fig. 1). As can be seen from Table 1 (page 800), the polymerases have different amino acid sequences and properties. Brautigam et al. (Curr. Opinion Struct. Biology, vol. 8, pp. 54-63, 1998) presented a review of known structures of DNA and RNA polymerases. Even though the

polymerases in general share certain similarities of the polymerase domain, the details of the structures differ from polymerase to polymerase even within a single family (Fig. 2; page 58, fifth paragraph; page 62, last paragraph).

Therefore, since the structure of any given protein is influenced by all of its components, introduction of mutations or additional structural elements is by no means routine in terms of obtaining a functional protein. This is supported by evidence provided by Barnes (U.S. Patent No. 5,436,149 A), which discloses construction of a thermostable DNA polymerase which can remain functional above 97° C. The constructs involved deletions of amino acids 1-278, 1-288 and 1-291 of Thermus aquaticus DNA polymerase (col. 5, lines 60-68; col. 6, lines 1-55), and the best result was obtained with a polymerase which had residues 1-278 removed (Fig. 4, for example). Therefore, deletion of only additional 10 or 13 amino acids markedly changed the thermostability properties of the enzyme. As stated by Barnes (col. 1, lines 67 and 68; col. 2, lines 1-17):

"The development of other enzymatically active mutein derivatives of Thermus aquaticus DNA polymerase is hampered, however, by the unpredictability of the impact of any particular modification on the structural and functional characteristics of the protein. Many factors, including potential disruption of critical bonding and folding patterns, must be considered in modifying an enzyme and the DNA for its expression. A significant problem associated with the creation of N-terminal deletion muteins of high-temperature Thermus aquaticus DNA polymerase is the prospect that the amino-terminus of the new protein may become wildly disordered in the higher temperature ranges, causing unfavorable interactions with the catalytic domain(s) of the protein, and resulting in denaturation."

In conclusion, any modification of a protein structure requires extensive testing to verify that the desired properties are obtained and that the protein retains its funtion.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied to produce claimed polymerases, including selection of possible anchoring sites for each of the polymerases, different types of anchors (peptides, nucleic acids, etc), influence of the modification on the protein structure and processivity, influence of reaction conditions (pH, temperature, type of nucleotides used). This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the structure and properties of a modified polymerase depend upon numerous known and unknown parameters such as the influence of each residue on the protein stability and function, potential tertiary structure changes affecting function under certain reaction conditions, the factor of unpredictability weighs heavily in favor of undue experimentation. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 112, second paragraph

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 1-3, 18, 19, 22, 23 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 18, 19, 22, 23 and 26 are indefinite in claim 1. Claim 1 is indefinite over the recitation of "wherein said polymerase has an attachment complex comprising at least one anchor covalently attached thereto". It is not clear what the anchor is attached to: the polymerase or the attachment complex.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

20. Claims 1-3, 18 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS and in the previous office action).

Regarding claims 1 and 26, Motz et al. teach a Taq polymerase-nucleic acid complex, where the polymerase comprises a PCNA-binding domain (= anchor) covalently attached to the polymerase and PCNA assembled on the binding domain (=attachment complex), which irreversibly associates the polymerase with the nucleic acid with the nucleic acid during the replication phase to increase

processivity (Abstract; page 16180, second paragraph; page 16181, third and last paragraphs; page 16183, second paragraph; page 16186, second and third paragraphs; Fig. 4). Motz et al. teach a Taq DNA polymerase with a PCNA binding motif (=an anchor), which is modified at its N-terminus by the presence of a six amino acid linker and 42 amino acid polB C-terminal amino acids (Fig. 4A).

Regarding claim 2, Motz et al. teach primers for the target nucleic acid (page 16181; third paragraph).

Regarding claim 3, Motz et al. teach a six amino acid linker and the PCNA-binding domain, therefore they teach two anchors (page 16183, second paragraph).

Regarding claim 18, Motz et al. teach circular DNA (page 16181; third paragraph).

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS and in the previous office action) and Blanco et al. (U.S. Patent No. 5,198,543 A; cited in the previous office action).

A) Motz et al. teach Taq DNA polymerase, but do not teach strand displacement synthesis or polymerases of claim 22.

B) Blanco et al. teach using phi29 DNA polymerase for strand displacement amplification and sequencing (col. 1, lines 9, 10; col. 2, lines 3-35; col. 4, lines 18-52; col. 8, lines 46-51 and 54-57).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the phi29 DNA polymerase of Blanco et al. as a polymerase of Motz et al. Blanco et al. specifically teach that phi29 polymerase can be used in place pf a Taq polymerase (col. 8, lines 54-57). The motivation to do so, provided by Blanco et al., would have been that the polymerase did not require temperature cycling and produced long strands of DNA (col. 8, lines 46-51).

23. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (U.S. Patent No. 6,255,083 B1; cited in the previous office action) and Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS and in the previous office action).

A) Regarding claim 23, Williams teaches sequencing of nucleic acids using DNA polymerases immobilized on solid supports and Klenow DNA polymerase (col. 2, lines 16-36; col. 14, lines 21-58) as well as Taq polymerase (col. 17, lines 43-58). Williams does not teach irreversible association of the polymerase with nucleic acid target.

B) Motz et al. teach a Taq polymerase-nucleic acid complex, where the polymerase comprises a PCNA-binding domain (= anchor) covalently attached to the polymerase and PCNA assembled on the binding domain (=attachment complex), which irreversibly associates the polymerase with the nucleic acid with the nucleic acid during the replication phase to increase processivity (Abstract; page 16180, second paragraph; page 16181, third and last paragraphs; page 16183, second paragraph; page 16186, second and third paragraphs; Fig. 4). Motz et al. teach a Taq DNA polymerase with a PCNA binding motif (=an anchor), which is modified at its N-terminus by the presence of a six amino acid linker and 42 amino acid polB C-terminal amino acids (Fig. 4A).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the modified Taq polymerase of Motz et al. in the nucleic acid sequencing

method of Williams. The motivation to do so, provided by Motz et al., would have been that the modification increased the Taq polymerase processivity (page 16186, second paragraph; Fig. 4).

Double Patenting

24. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

25. Claims 1-3, 23 and 26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 19 of U.S. Patent No. 7,462,468 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 19 discloses the claimed polymerase-nucleic acid complex of claims 1, 2, 23 and 26.

Specifically, claim 1 of the instant application is drawn to a polymerase-nucleic acid complex for increasing the processivity index, said polymerase-nucleic acid complex comprising: a target nucleic acid and a nucleic acid polymerase, wherein said polymerase has an attachment complex comprising at least one anchor covalently attached thereto, said at least one anchor having a modified amino acid, wherein during replication, said attachment complex irreversibly associates said target

nucleic acid with said polymerase until the replication is complete, thereby increasing the processivity index.

Claim 19 of the '468 patent is drawn to a method for detecting incorporation of at least one nucleotide phosphate into a single primer nucleic acid molecule, said method comprising:

i. immobilizing onto a support a polymerase nucleic acid complex comprising a target nucleic acid, a primer nucleic acid which complements a region of the target nucleic acid, and at least one nucleic acid polymerase;

ii. contacting said immobilized complex with at least one type of labeled nucleotide phosphate of the formula II: (omitted) wherein:

Dye^1 is selected from the group consisting of TO-1, TO-3, BO-1, BO-3, YO-1, YO-3, JO-1, JO-3, PO-1, PO-3, LO-1, LO-3, YO-1, YO-3, propidium and psoralen;

Dye^2 is selected from the group consisting of TO-1, TO-3, BO-1, BO-3, YO-1, YO-3, JO-1, JO-3, PO-1, PO-3, LO-1, LO-3, YO-1, YO-3, propidium and psoralen;

r is 1-6;

t is 1-6;

n is 0-20;

Z is a member selected from the group consisting of O, S, CR^1R^2, NR^3R^4, and $P(O)_2$;

R^1, R^2, R^3, and R^4 are each members independently selected from the group consisting of H and optionally substituted alkyl; L is a member selected from the group consisting of a direct link, or a covalent linkage, wherein said covalent linkage is linear or branched, cyclic or heterocyclic, saturated or unsaturated, having 1-100 atoms selected from the group consisting of C, N, P, O, and S, wherein L can have additional hydrogen atoms to fill valences, and wherein said linkage contains any combination of ether, thioether, amine, ester, carbamate, urea, thiourea, oxy or amide bonds; or single,

double, triple or aromatic carbon-carbon bonds; or phosphorus-oxygen, phosphorus-sulfur, nitrogen-nitrogen, nitrogen-oxygen, or nitrogen-platinum bonds; or aromatic or heteroaromatic bonds; and NP is a nucleotide phosphate [NP]; and

iii. detecting the incorporation of said at least one type of labeled NP into a single molecule of said primer, while said at least one type of labeled NP is in contact with said immobilized complex, by detecting the label of the NP while said at least one type of labeled NP is in contact with said polymerase nucleic acid complex, wherein said polymerase-nucleic acid complex comprises a target nucleic acid and a nucleic acid polymerase, wherein said polymerase has an attachment complex comprising at least one anchor, which irreversibly associates said target nucleic acid with said polymerase for increasing the processivity index.

The specification describes covalent anchors and more than two anchors in col. 19, lines 59-67 and col. 19.

Therefore the polymerase nucleic acid complex of claims 1-3, 23 and 26 is anticipated by claim 19 of the 7,462,468 patent.

26. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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